Adjuvant Chemotherapy and de-escalation

NICE GUIDANCE

Anthracycline + Takane Regimens:
o Commonly used regimens in adjuvant therapy include anthracyclines (e.g., epirubicin or doxorubicin) and taxanes (e.g., paclitaxel or docetaxel). Anthracyclines are associated with side effects like cardiac toxicity and nausea, while taxanes increase risks like neuropathy, neutropenia, hypersensitivity, and alopecia.
o The combination of these agents improves outcomes in high-risk patients but comes with a trade-off in toxicity profiles. This should always be discussed with the patient.

Cyclophosphamide or Cisplatin Use:
o Cyclophosphamide is commonly added to anthracycline/taxane regimens in patients with a high risk of recurrence.
o Cisplatin is less commonly used in adjuvant therapy but can be considered for high-risk cases, particularly in TNBC patients, though this may not be the standard for all patients

Risk Stratification Using Tools

o NPI (Nottingham Prognostic Index) can help guide treatment decisions. NPI scores of 3.4–5.4 place patients in an intermediate-risk group, where chemotherapy, may be beneficial.

o PREDICT and Adjuvant Online are tools used to predict the benefit of chemotherapy, though PREDICT may have limitations in younger patients (under 30 years), in ER+ patients over 70 years, bilateral breast cancer, in tumours >5 cm. It has not been validated in men or certain ethnic minorities, but it is widely used in the UK. While PREDICT is a useful tool, clinicians need to be aware of these limitations and should use it in conjunction with other clinical judgment, genomic testing, and patient-specific factors for more tailored treatment decisions.

Oncotype DX:

o Oncotype DX is a genomic assay recommended for patients with ER+, HER2-, LN+ or LN- breast cancer. It is useful in determining the benefit of adjuvant chemotherapy, especially in intermediate-risk patients.
o For LN- patients, Oncotype DX is recommended primarily if they are considered high-risk based on other factors like PREDICT or tumour characteristics.

Special Considerations:

o For LN0 patients, chemotherapy may be offered based on other risk factors, such as a high score on PREDICT or unfavourable tumour biology.
o It's important to balance the risks and benefits of chemotherapy, particularly in older patients or those with comorbidities.

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Key trials for de-escalation

- TailorX 2018- 10k patients 3 groups:
  1) Score 11-25 oncotype randomised to chemo-endocrine or endocrine alone (4k)
  2) Low risk <11 chemo omitted [building on Plan-B which removed anthracycline from EC-T]
  3) high risk>25 given chemo.

  9 yr OS in LN0 RS 11-25 was 94% with or without chemotherapy so justified that in N0 patients could omit chemo if intermediate score. But caution if <51yrs and if 11-15 score (underpowered) and may benefit. Raised the question can we omit in node positive ER+ disease, hence RxPonder

- RxPONDER trial confirmed that we can omit adjuvant chemotherapy in post-menopausal woman with hormone receptor–positive, HER2-negative disease, one to three positive lymph nodes, and a 21-gene Oncotype DX recurrence score (RS) of 0 to 25.
Pre-menopausal is more difficult as rates of OFS were different in each arm and we now have CDK4/6- available for high rx ER+. Non-inferiority trial so caution with interim!

- The St. Gallen 2021 consensus statements reflect expert opinions on various breast cancer treatment strategies. Below is a refined and corrected version of the points you've mentioned, aligned with the St. Gallen guidelines:

• 98% agreement that postmenopausal women with low-grade, early-stage breast cancer and/or low-risk genomic scores do not require chemotherapy. This reflects the belief that endocrine therapy alone is sufficient in such low-risk cases.

• 73% agreement that genomic testing on core biopsy samples can be used to help identify patients with ER-positive (ER+) breast cancers who may not need chemotherapy. Genomic assays like Oncotype DX or MammaPrint help stratify patients based on recurrence risk and the likely benefit of chemotherapy.

• 84% agreement that for HER2-positive (HER2+), node-negative breast cancer patients, there is no need for anthracyclines if they are receiving a combination of taxane-based chemotherapy and anti-HER2 therapy (e.g., trastuzumab). In the case of node-positive HER2+ patients, opinions were divided, with some experts recommending anthracyclines and others preferring to avoid them, depending on the clinical situation.